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EXAMINER	
WAX, ROBERT A	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,828	MOSER ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-20* is/are pending in the application.

4a) Of the above claim(s) *3,13,14 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,14,15,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05102004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Introduction

1. This Office action is responsive to the amendment filed May 10, 2004. Applicants' amendments and arguments are sufficient to overcome the rejection under 35 USC 101 and parts of the rejection under 35 USC 112, first paragraph, written description. However, not all of the written description rejection has been overcome and the withdrawal of the rejection under 35 USC 101 necessitates expansion of the previous rejections under 35 USC 112, first paragraph, enablement. New rejections for lack of enablement and some new rejections under 25 USC 112, second paragraph are deemed necessary as well. Since not all new grounds of rejection were necessitated by amendment, the instant Office action is made nonfinal.

Information Disclosure Statement

2. The information disclosure statement filed May 10, 2004 has been considered. Please see the attached initialed PTO-1449.

Claim Objections

3. Claims 1, 6, 9 and 20 are objected to because of the following informalities: Claims 1 and 20 use the phrase, "where the amino acids in parantheses (sic) are not mandatorily present" but claim 6 states, "need not necessarily be present." Use of the

same language in all the claims would enhance the clarity. Of course, "parantheses" is misspelled also. Claim 9 is missing a comma after the word, "immunogen". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Written Description

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 4, 5, 10-12 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to claims 4, 5 and 19, the specification lacks adequate written description of the "conformation" sequence. As explained in the previous Office action, the specification, while briefly discussing conformation sequences at pages 5 and 6, contains no disclosure of what sequences may be styled as conformation sequences that induce the formation of a defined conformation of PrP. The instant claims are directed to peptides coupled with a "conformation" sequence where the claimed product is defined by its functional characteristics (i.e., the claimed peptides coupled with

conformation sequences simulate the spatial conformation in the PrP^{Sc} protein). The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original).

Just as the claims at issue in *UC v. Lilly* defined the invention by the function of the claimed DNA (encoding insulin), the instant claims define the claimed products only by their functional properties. The court held this sort of functional definition insufficient. "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to

define the genus because it is only an indication of what the gene does, rather than what it is." *UC v. Lilly*, at *24-*25. Thus, claims 4, 5 and 19 lack adequate written description of the "conformational" sequences.

With regard to claims 10-12, the specification lacks adequate written description of any PrP^{Sc} binding substances except for antibody 15B3. The previous Office action stated

> One basic piece of information is not disclosed and that is what exactly the PrP^{Sc}-binding substances are. A single antibody has been disclosed but it is unclear to what portion of the PrP that the antibody binds to and it has not been established that it is specific for the Sc conformation. The area of prion proteins is extremely murky and nobody seems to know exactly what is going on.

The references provided by applicants establish that antibody 15B3 does, in fact, bind to PrP^{Sc} but no other PrP^{Sc} binding substances have been disclosed.

Claims 10-12 are directed to methods utilizing one or more PrP^{Sc}-binding substances where said substances are defined by their functional characteristic of binding to PrP^{Sc}. The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at

*23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original).

Just as the claims at issue in *UC v. Lilly* defined the invention by the function of the claimed DNA (encoding insulin), the instant claims define the binding substances used in the claimed methods only by their functional properties. The court held this sort of functional definition insufficient. "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." *UC v. Lilly*, at *24-*25. By extension, a method of use of a substance that lacks adequate written description must also lack sufficient written description. Thus, claims 10-12 lack adequate written description of the PrP^{Sc}-binding substances.

Claim Rejections - 35 USC § 112, Enablement

6. Claims 4, 5, 7, 10, 15 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 4, 5 and 19 contain the language, "in such a manner as to simulate the spatial conformation in the PrP^{Sc} protein", "induces the formation of a β strand" and "in such a manner as to attain a PrP^{Sc}-specific epitope with at least two spatially neighboring binding sites." The specification is devoid of any disclosure at all as to how these goals are to be attained. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single,

simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case, (1) the amount of experimentation is large because of the unlimited number of possible "conformational sequences" that might be chosen; (2) the amount of guidance provided by the specification is zero since the properties that determine what protein might contain a conformational sequence are not disclosed. One of skill in the art would have no idea what structural characteristics might make one peptide be a conformational sequence and another not. Thus, one of skill in the art would have no idea as to where to even begin, much less define a plan of research. Continuing, (3) the specification is totally devoid of any working examples; as for the next Wands factor, (4) the nature of the invention is the discovery of an antibody that recognizes PrP^{Sc}, which appears to be the first (and only, as of 2004) such identified PrP^{Sc}-binding substance. The prior art (5) shows that PrP is known, that terrible illnesses are caused by the unexplained change in conformation from PrP to PrP^{Sc} and that nobody knows what causes the change in conformation; (6) the relative level of skill in this art is very high; (7) the predictability of the art is nonexistent since nobody has been able to find a PrP^{Sc}-binding substance except for, presumably, antibody 15B3.

Finally, (8) the claims are enormously broad because the conformational sequence could be any peptide of any length and having any sequence.

Based on this analysis, the conclusion that it would require undue experimentation to practice the instant invention as defined in claims 4, 5 and 19 is inescapable.

Claim 7 recites polypeptides of claim 1 wherein part of the sequence is present in the retro form. The specification is devoid of any disclosure at all as to which amino acids may be in the retro form or how many may be in the retro form. This recitation amounts to reciting nonspecified mutants since a partly retro sequence differs from the original. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art.

The factors to be considered have been outlined above.

In the case of claim 7, (1) the amount of experimentation is large because of the large number of possible combinations of retro portions of the sequences that might be chosen; (2) the amount of guidance provided by the specification is zero since the no such sequence containing a retro portion is disclosed. One of skill in the art would have no idea of which amino acids could be changed around without affecting the properties of the protein, much less have an idea as to what logical progression of alterations might be made to determine if the protein is still functional. The specification also provides no guidance regarding, for example, the domain structure of the protein, the location of the active site, or sites of interaction with other proteins, cofactors or

regulatory molecules. In order to predict with reasonable assurance the effect that different alterations are likely to have on the protein, and thereby predict which mutants will retain biological activity, the skilled artisan would require data regarding, for example, the molecular basis of the protein's activity, its secondary and tertiary structure and the relative importance of any domains of the protein in maintaining said activity. None of this type of information is present in the instant specification. Continuing, (3) the specification is totally devoid of any working examples; as for the next Wands factor, (4) the nature of the invention is the discovery of an antibody that recognizes PrP^{Sc}, which appears to be the first (and only, as of 2004) such identified PrP^{Sc}-binding substance. The prior art (5) shows that PrP is known, that terrible illnesses are caused by the unexplained change in conformation from PrP to PrP^{Sc} and that nobody knows what causes the change in conformation; (6) the relative level of skill in this art is very high; (7) the predictability of the art is low since nobody can predict the effect different alterations might have on the protein. Finally, (8) the claims are enormously broad because the number of possible alterations is large.

Based on this analysis, the conclusion that it would require undue experimentation to practice the instant invention as defined in claim 7 is inescapable.

Claim 10 recites a pharmaceutical composition comprising either the synthetic isolated polypeptide or at least one PrP^{Sc}-binding substance recognizing said polypeptide at a dosage adequate for therapy or prevention. This claim lacks enablement for three reasons. First, the only PrP^{Sc}-binding substance disclosed is antibody 15B3 and the administration of antibodies for therapy is notoriously

unpredictable, second, it would require undue experimentation to locate other PrP^{Sc}-binding substances that would be active in treating prion diseases, third, it would not be possible to determine the dosage of either peptide or PrP^{Sc}-binding substance necessary for prevention of prion disease without undue experimentation. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art.

The factors to be considered have been outlined above and they will be discussed for each aspect of this rejection of claim 10.

With regard to the first reason, namely, that the only PrP^{Sc}-binding substance disclosed is antibody 15B3 and the administration of antibodies for therapy is notoriously unpredictable, (1) the amount of experimentation is small because only one antibody need be tested; (2) the amount of guidance provided by the specification is zero since no treatment is disclosed. Antibody administration must take into account variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The antibody may be inactivated *in vivo* before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half-life of the formulation. In addition, the antibody may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the antibody has no effect, circulation into the target area may be insufficient to carry the antibody and a large enough local concentration may not be established. No

guidance as to how to counteract these variables has been presented. In addition, it is unclear what antibody 15B3 will do even if it gets to its intended site. There is no evidence as to how PrP^{Sc} causes prion diseases and even binding the antibody to the protein might do nothing to interfere with the unknown activity of the protein. Continuing, (3) the specification is totally devoid of any working examples; as for the next Wands factor, (4) the nature of the invention is the discovery of an antibody that recognizes PrP^{Sc}, which appears to be the first (and only, as of 2004) such identified PrP^{Sc}-binding substance. The prior art (5) shows that PrP is known, that terrible illnesses are caused by the unexplained change in conformation from PrP to PrP^{Sc} and that nobody knows what causes the change in conformation; (6) the relative level of skill in this art is very high; (7) the predictability of the art is low since nobody can predict whether the antibody will reach its intended target or even do anything to counteract the protein's activity if it does reach it. Finally, (8) the claims are not particularly broad, again, because only a single antibody need be tested.

Based on this analysis, the conclusion that it would require undue experimentation to use the claimed pharmaceutical composition to treat prion disease by administration of antibody 15B3 is inescapable.

With regard to the second reason, namely, that it would require undue experimentation to locate other PrP^{Sc}-binding substances that would be active in treating prion diseases, (1) the amount of experimentation is immense because the number of substances that must be selected and tested is virtually limitless; (2) the amount of guidance provided by the specification is zero since only the single PrP^{Sc}-

binding substance is disclosed. Information such as the structure of the binding region is needed to even begin to outline a research plan and no such information has been presented. Continuing, (3) the specification is totally devoid of any working examples; as for the next Wands factor, (4) the nature of the invention is the discovery of an antibody that recognizes PrP^{Sc}, which appears to be the first (and only, as of 2004) such identified PrP^{Sc}-binding substance. The prior art (5) shows that PrP is known, that terrible illnesses are caused by the unexplained change in conformation from PrP to PrP^{Sc} and that nobody knows what causes the change in conformation; (6) the relative level of skill in this art is very high; (7) the predictability of the art is low since nobody can predict which substances might bind PrP^{Sc}. Finally, (8) the claims are extremely broad, again, because the number of possible PrP^{Sc}-binding substances is unlimited.

Based on this analysis, the conclusion that it would require undue experimentation to use the claimed pharmaceutical composition to treat prion disease by administration of an undefined PrP^{Sc}-binding substance is inescapable.

The third reason that claim 10 is not enabled is that it would not be possible to determine the dosage of either peptide or PrP^{Sc}-binding substance necessary for prevention of prion disease without undue experimentation. This would require administration of the claimed peptide or PrP^{Sc}-binding substance prior to the development of the prion disease. Turning to the Wands factors, (1) the amount of experimentation is immense because, for example, the number of variables that might determine susceptibility to prion disease is unknown, the number of PrP^{Sc}-binding substances that must be selected and tested is virtually limitless and the length of time

needed for the experimentation is undefinable since susceptibility might not manifest for years; (2) the amount of guidance provided by the specification is zero since there is no guidance in the specification for determining the appropriate time prior to the development of the prion disease to begin the therapy or for identifying patients at risk for developing prion diseases. Continuing, (3) the specification is totally devoid of any working examples; as for the next Wands factor, (4) the nature of the invention is the discovery of an antibody that recognizes PrP^{Sc}, which appears to be the first (and only, as of 2004) such identified PrP^{Sc}-binding substance. The prior art (5) shows that PrP is known, that terrible illnesses are caused by the unexplained change in conformation from PrP to PrP^{Sc} and that nobody knows what causes the change in conformation; (6) the relative level of skill in this art is very high; (7) the predictability of the art is zero since the factors defining susceptibility to prion disease are unknown. Finally, (8) the claims are extremely broad, again, because the number of variables to define and test for is immense.

Based on this analysis, the conclusion that it would require undue experimentation to use the claimed pharmaceutical composition to prevent prion disease by administration of one of the peptides, antibody 15B3 or an undefined PrP^{Sc}-binding substance is inescapable.

Claim 15 recites a kit to detect PrP^{Sc} or antibodies recognizing it comprising a polypeptide of claim 1. This is deemed to be nonenabled for two reasons. First, Page 9 of the specification states,

> As already mentioned, one of the substances used to ascertain the polypeptide sequences may be recombinant bovine rbPrP. Surprisingly it

> was found that recombinant rbPrP is able to specifically bind to PrP^{Sc} and to recognize, at the corresponding peptide bank, the same sequences as the antibodies 15B3 (see Fig. 2).

Nothing has been shown as to whether the specific polypeptides of claim 1 will bind to PrP^{Sc} and the fact that rbPrP recognizes PrP^{Sc} does not establish that the specific polypeptides of claim 1 will behave similarly. This finding is buttressed by applicants' own assertion that this was a surprising result; by definition, a surprising result does not enable one to make predictions based on that result. Examiner is quite surprised that the PrP conformer binds the PrP^{Sc} conformer at all and would be more surprised if the specific polypeptides of claim 1 behave similarly. Second, the only antibody to PrP^{Sc} yet discovered is 15B3 and it would require undue experimentation to find others. The Wands analysis for this point is the same as outlined above for the second reason why claim 10 lacks enablement.

7. Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnostic means comprising antibody 15B3, does not reasonably provide enablement for diagnostic means using the polypeptides of claim 1 or other, undisclosed, PrP^{Sc}-binding substances. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not

enabling for claims drawn to diagnostic means using the polypeptides of claim 1 or other, undisclosed, PrP^{Sc}-binding substances.

The Wands analysis for this point is the same as outlined above for the second reason why claim 10 lacks enablement.

Based on this analysis, the conclusion that it would require undue experimentation to practice the instant invention is inescapable.

Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 4, 6, 9, 11, 12 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 19 are rendered indefinite by the phrase, "where applicable" since the conditions under which the use of the spacer is applicable are not defined.

Regarding claim 6, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 11 and 12 use language unusual to diagnostic means claims to such a degree as to render the claims indefinite. The use of the word "dose" with "sufficient for the particular detection" or "sufficient for immunization" is the cause of the

indefiniteness. In claim 11 the idea is that the polypeptide of claim 1 or the PrP^{Sc}-binding substance will somehow detect prion disease and, therefore, permit diagnosis of it. The word "dose" is usually used for compositions intended for treatment of diseases. In claim 12 it is not clear that the polypeptide of claim 1 or the PrP^{Sc}-binding substance is immunizing anything. The term "immunizing" has an art-accepted meaning, which is

> Protection of susceptible individuals from communicable diseases by administration of a living modified agent (*e.g.,* yellow fever vaccine), a suspension of killed organisms (*e.g.,* pertussis vaccine), or an inactivated toxin (*e.g.,* tetanus). From Stedman's Online Medical Dictionary.

The intent of claim 12 has nothing to do with protection from communicable diseases and, therefore, the claim is indefinite.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 4, 5, 10-12 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Prusiner et al.

Prusiner et al. teach a polypeptide having SEQ ID No. 3: their SEQ ID No. 2, residues 125-137, wherein R7=Thr, R8=Gln, R9=Lys, R10=Ser, R11=Tyr and their SEQ ID No. 10, residues 125-137, wherein R7=Ile, R8=Glu, R9=Arg, R10=Gln, R11=Tyr.

This clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. Applicants are referred to Table 1 on page 34 or Prusiner et al., specifically to the entry for SHa 90-231. Instant SEQ ID No. 3 is present near the end (CTTQYQKESQAYY) but the amino acids preceding this sequence read on the claimed "conformation" sequence.

12. Claims 1, 4, 5, 10-12 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Loftus et al.

Loftus et al. teach a polypeptide having SEQ ID No. 3: see Fig. 1, residues 213-225, wherein R7=Ile, R8=Gln, R9=Gln, R10=Gln, R11=Ala. This clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 213-225 read on the claimed "conformation" sequence.

13. Claims 1, 4, 5, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank locus UJHYIH.

UJHYIH teaches a polypeptide having SEQ ID No. 3: see residues 214-226, wherein R7=Thr, R8=Gln, R9=Lys, R10=Gln, R11=Tyr. This clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 214-226 read on the claimed "conformation" sequence.

14. Claims 1, 4, 5, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by EMBL accession number U75383.

U75383 teaches a polypeptide having SEQ ID No. 3: see residues 199-211, R7=Ile, R8=Gln, R9=Lys, R10=Gln, R11=Tyr. This clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 199-211 read on the claimed "conformation" sequence.

15. Claims 1, 4-6, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Liao et al.

Liao et al. teach a polypeptide having SEQ ID No. 3: see Fig. 3, rat and mouse sequences, residues 225-237 (based on the human sequence), wherein R7=Val, R8=Gln, R9=Lys, R10=Gln, R11=Tyr; hamster sequence, residues 225-237 (based on the human sequence), wherein R7=Thr, R8=Gln, R9=Lys, R10=Gln, R11=Tyr and the human sequence, residues 225-237, wherein R7=Ile, R8=Glu, R9=Arg, R10=Gln, R11=Tyr. This clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 225-237 read on the claimed "conformation" sequence.

Liao et al. also teach a polypeptide having SEQ ID No. 4: see Fig. 3, rat sequence, residues 161-172 (based on the human sequence), wherein R12=Tyr. This

clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 161-172 read on the claimed "conformation" sequence.

Liao et al. also teach a polypeptide having SEQ ID No. 10: see Fig. 3, human, rat, hamster and mouse sequences, residues 130-040 (based on the human sequence), wherein R13=Met. This clearly anticipates claim 6 since that claim recites a polypeptide containing the defined sequence.

16. Claims 1, 4, 5, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Locus UJHU.

UJHU teaches a polypeptide having SEQ ID No. 4: see residues 150-162, wherein R12=His. This clearly anticipates claims 1, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 150-162 read on the claimed "conformation" sequence.

17. Claims 1, 4-6, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Cervenáková et al.

Cervenáková et al. teach a polypeptide having SEQ ID No. 2: see Figure 1, squirrel monkey sequence, residues 159-171, wherein R3=Lys, R4=Val, R5=Gln, R6=Ser and gorilla sequence, residues 160-172, wherein R3=Arg, R4=Met, R5=Gln, R6=Ser. They also teach a polypeptide having SEQ ID No. 11, see Figure 1, gorilla

sequence, residues 162-172, R3=Arg, R4=Met, R5=Gln, R6=Ser. This clearly anticipates claims 1, 6, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 159-171, 160-172 and 162-172, respectively, read on the claimed "conformation" sequence.

18. Claims 1, 4-6, 10-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Schätzl et al.

Schätzl et al. teach a polypeptide having SEQ ID No. 1: see Figure 2, spider monkey sequence, residues 126-134, wherein R1=Asn, R2=Tyr. They also teach a polypeptide having SEQ ID No. 3, see Figure 2, spider monkey sequence, residues 198-210, wherein R7=Ile, R8=Gln, R9=Arg, R10=Gln, R11=Tyr and night monkey sequence, residues 206-218, wherein R7=Ile, R8=Glu, R9=Lys, R10=Gln, R11=Tyr. This clearly anticipates claims 1, 6, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as well. The amino acids preceding residues 126-134, 198-210 and 206-218, respectively, read on the claimed "conformation" sequence.

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 1, 4-12, 15 and 20 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fishleigh et al.

Fishleigh et al. teach a polypeptide having SEQ ID No. 1: see their SEQ ID No. 42, residues 11-19, wherein R1=Asn, R2=Tyr; their SEQ ID No. 43, residues 11-19, wherein R1=Ser, R2=Tyr, their SEQ ID No. 10, residues 11-19, wherein R1=Ser, R2=Tyr their SEQ ID No. 11, residues 11-19, wherein R1=Ser, R2=Tyr and their SEQ ID No. 12, residues 11-19, wherein R1=Ser, R2=Tyr. They also teach a polypeptide having SEQ ID No. 2, see their SEQ ID No. 13, residues 8-20, wherein R3=Arg, R4=Val, R5=Gln, R6=Ser, their SEQ ID No. 14, residues 8-20, wherein R3=Arg, R4=Val, R5=Arg, R6=Ser, their SEQ ID No. 15, residues 8-20, wherein R3=Arg, R4=Met, R5=Glu, R6=Ser, their SEQ ID No. 44, residues 8-20, wherein R3=Arg, R4=Val, R5=Arg, R6=Ser, their SEQ ID No. 45, residues 8-20, wherein R3=Arg, R4=Val, R5=Gln, R6=Ser, their SEQ ID No. 16, residues 8-20, wherein R3=Arg, R4=Val, R5=Gln, R6=Ser, their SEQ ID No. 17, residues 8-20, wherein R3=Arg, R4=Val, R5=Arg, R6=Ser and their SEQ ID No. 18, residues 8-20, wherein R3=Arg, R4=Met, R5=Glu, R6=Ser. They also teach a polypeptide having SEQ ID No. 11, see their SEQ ID No. 44, residues 10-20, wherein R3=Arg, R4=Val, R5=Arg, R6=Ser and their SEQ ID No. 45, residues 10-20, wherein R3=Arg, R4=Val, R5=Gln, R6=Ser. This clearly anticipates claims 1, 6, 10-12 and 15 since each claim recites a polypeptide containing the defined sequence. Claims 4 and 5 are considered to be anticipated as

well. The amino acids preceding the designated residues reading on the instant SEQ ID Nos., respectively, read on the claimed "conformation" sequence.

Fishleigh et al. teach the retro form at page 23, lines 14-22, thus anticipating claim 7. They teach that some of the residues may be in the D form at page 21, lines 28-29, thus anticipating claim 8. They teach the polypeptide bound to a carrier at page 24, line 37-page 25, line 32, thus anticipating claim 9. They teach antigenically significant sub fragments at page 21, lines 20-25, thus anticipating claim 20.

Alternatively, should the teachings of Fishleigh et al. not anticipate claims 7-9 and 20, it would have been obvious to one of ordinary skill in the art at the time the invention was made to follow the teachings of the reference with regard to retro portions, D-amino acids, carrier and subfragments to thus arrive at the polypeptides claimed in claims 7-9 and 20 with the expectation of beneficial results.

Claim Rejections - 35 USC § 103

21. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fishleigh et al.

The teachings of Fishleigh et al. have been outlined above. At page 27, lines 29-32 they teach of a kit comprising at least one synthetic polypeptide according to the invention. It would have been obvious to one of ordinary skill in the art at the time the invention was made to couple two of the antigenic polypeptides together with the expectation of isolating two antibodies at the same time, one that recognizes each of

the polypeptides in the conjugated molecule. Generation of multiple antibodies with multiple epitopes is standard practice in the antibody art and one of ordinary skill in that art would follow the standard practice.

Response to Arguments

22. Applicant's arguments filed May 10, 2004 have been fully considered but they are not all persuasive. As stated above, the arguments and references are effective to remove the rejection under 35 USC 101 and the rejection under 35 USC 112, first paragraph that went with it. However, the rejections under 35 USC 112, first paragraph with regard to written description are maintained and expanded upon. The arguments against the prior rejection under 35 USC 102(b) are effective, Examiner must agree that isolated protein does not occur naturally. However, please note the new rejections made under 35 USC 102(a) and (b), and 103(a) above.

Conclusion

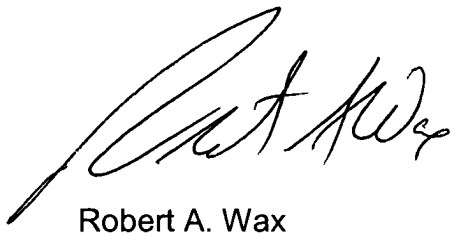
23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (571) 272-

0623. The examiner can normally be reached on Monday through Friday, between 9:00 AM and 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Robert A. Wax
Primary Examiner
Art Unit 1653

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